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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/799,291	03/12/2004	Farooq Uraizee	NVI 5275	8211

321 7590 05/07/2007

SENNIGER POWERS
ONE METROPOLITAN SQUARE
16TH FLOOR
ST LOUIS, MO 63102

EXAMINER	
OGUNBIYI, OLUWATOSIN A	

ART UNIT	PAPER NUMBER
1645	

NOTIFICATION DATE	DELIVERY MODE
05/07/2007	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/799,291	URAIZEE ET AL.	
	Examiner	Art Unit	
	Oluwatosin Ogunbiyi	1645	

-- *The MAILING DATE of this communication appears on the cover sheet with the correspondence address* --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 February 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-27* is/are pending in the application.

4a) Of the above claim(s) *3 (inpart), 6 (in part) and 7 (in part)* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 2, 3 in-part, 4, 5, 6 in-part, 7 in-part, 8 - 27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *3/12/2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *8/16/2004*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-27 are pending in the application. Claims 1-2, 3 in-part, 4-5, 6 in-part, 7 in-part, 8-26 and 27 in-part are instantly under examination.

Election/Restrictions

Applicant(s) election of the species; (1) combination of *Eimeria acervulina, Eimeria maxima* and *Eimeria tenella* and (2) tween 20 in the reply filed 2/12/2007 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). Claims 3 in-part, 6 in-part, 7 in-part and 27 in-part are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected specie, there being no allowable generic or linking claim.

Priority

Applicant(s) claim for domestic priority under 35 U.S.C. 119(e) and 35 U.S.C. 120 is acknowledged. However, the provisional application 60/163,989 and non-provisional application 09/708,918 upon which priority is claimed does not provide support for claims 8-10 of the instant application. The claims are drawn to specific

concentrations of surfactant, which are not disclosed in the priority documents. Thus, claims 8-10 have the instant filing date of 3/12/2004.

Drawings

The drawings in this application have been accepted. No further action by Applicant is required.

Information Disclosure Statement

The information disclosure statement filed 8/16/2004 has been considered. An initialed copy is enclosed.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claims 25-27 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a preparation for the prevention of avian coccidiosis due to *Eimeria* comprising a pharmaceutically acceptable carrier, diluent or excipient, a subpathogenic dose of sanitized live sporulated oocysts of *Eimeria* and an amino acid or surfactant, does not reasonably provide enablement for a preparation for the treatment of avian coccidiosis, or the prevention and treatment of coccidiosis caused by other species of coccidia. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The claims are drawn to a preparation for the prevention and treatment of coccidiosis comprising live sporulated oocysts and an amino acid or surfactant.

Coccidiosis is defined as disease due to any species of coccidian, which is a common protozoan disease of many species of domestic animals, birds and many wild animals; both intestinal and pulmonary coccidiosis have been reported in humans with

AIDS (definition of coccidiosis from Stedmans Online Medical Dictionary, retrieved 4/11/07).

The nature of the instant invention and the breadth of the claims are broad as the claims require the both the prevention and treatment of coccidiosis caused by all species of coccidian (*Cryptosporidium* species, *Isospora* species, *Eimeria* Species, for example) that infect a variety of animals and as well as in humans. The claims also require the use of live viable sporulated oocysts to prevent coccidiosis as well as to treat ongoing coccidiosis.

Live oocyst vaccines of *Eimeria* are known in the art for prevention of avian coccidiosis caused by *Eimeria* species (Danforth et al. International Journal for Parasitology vol. 28, p. 1099-1109, 1998, Chapman et al. International Journal for Parasitology vol. 32, p. 617-629, 2001). Chickens exposed to said vaccine develop immunity to subsequent infection with *Eimeria* i.e. the chickens are deliberately exposed to the live oocysts so that immunity to natural infection is established early in life. As to treatment of coccidiosis, treatment requires that chickens already having coccidiosis are treated with live sporulated oocysts. The live oocyst vaccines taught in the art are administered to very young chickens (e.g. 1 day old) at subpathogenic doses to provide protective immunity against subsequent coccidiosis (see Danforth et al and Chapman et al). The art does not teach whether such live oocyst vaccines can be used to treat

coccidiosis i.e. ongoing disease in chickens. The specification does not correlate the administration of a preparation comprising live sporulated oocysts of *Eimeria* with the treatment of ongoing avian coccidiosis in chickens or other bird species.

As to coccidiosis caused by cryptosporidium sp., such a vaccine strategy may not be effective or practical especially for the immune-compromised (see abstract - Jenkins et al. Veterinary Parasitology vol.101, p.291-310, 2001). There are no effective drugs or preventive measures available for the control of coccidiosis caused by cryptosporidium (abstract Harp et al. J. Dairy Sci, 81:289-294, Tsang et al. US 6,475,747, 2002, column 2 lines 23-29) and vaccination therapy for *Cryptosporidium* still in its infancy is focused on the use of hyperimmune colostrums, antibodies, sporozoite antigens and DNA vaccination (Jenkins et al. p. 294 section 2.3). The art is silent at to whether administration of live viable sporulated oocysts is efficacious in prevention and treatment of coccidiosis caused by *Cryptosporidium* and the specification does not provide any evidence as to the efficacy of such method.

As to coccidiosis caused by *Isospora* and *Cyclospora*, such pathogens are associated with chronic diarrhea in HIV-infected persons (Verdier et al. Ann Intern Med. 2000; 132:885-888). Treatment is by administration of chemical drugs such as azoles or antibiotics. The art is silent as to the use of a live sporulated oocyst vaccine for the treatment and prevention of coccidiosis due to *Isospora* and *Cyclospora*. Similar to

cryptosporidium, such a vaccination strategy may not be practical especially for the immune-compromised and the specification does not correlate the administration of live sporulated oocysts from *Isospora* and *Cyclospora* with the treatment and prevention of coccidiosis due to these parasites any animal model or in a human. Thus, the efficacy of such a live vaccine for treatment and prevention is unpredictable.

The instant application is enabled for prevention of avian coccidiosis using a composition comprising live sporulated oocysts of *Eimeria* as set forth above. The efficacy of such a composition in preventing and treatment of other species of coccidia is unpredictable because it' s not clear whether cross species protection can occur. Furthermore, giving living sporulated oocysts of *Cryptosporidium* to an immunocompromised patient will not treat or prevent coccidiosis but will actually cause coccidiosis.

In summary, due to the nature of the invention and breadth of the claims, the limited teachings in the specification as to the treatment of avian coccidiosis with live sporulated oocysts, the treatment and prevention of non-avian coccidiosis using live sporulated oocysts and the silence of the art as to vaccination against non-avian coccidiosis using live sporulated oocysts, undue experimentation would be required of the skilled artisan to use the instant invention.

Claims 1-24 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

As to claims 1-24, the claims are drawn to a composition comprising viable sporulated oocysts... wherein the composition is sterile. The specification on p. 11 defines sterile to mean that there are no detectable amounts of live, viable, bacteria, viruses or fungi in the composition. The dictionary definition of sterile is free from germs (see attached sterile definition). Sterile as defined in the specification depends on the method of the detection of live, viable, bacteria, viruses or fungi. Because there are no detectable amounts of such microorganisms does not completely rule out the presence of said organisms. Therefore, in light of applicants definition of sterile, said composition can include some undetectable amounts of said microorganisms and therefore is contrary to the definition of sterile being free of germs. Applicants are respectfully requested to clarify sterile as defined in the specification as said definition allows undetectable amounts of live, viable bacteria, viruses, or fungi in the claimed *sterile* composition.

As to claim 14, the dosage unit of what sample, is the claim referring to?

As to claim 16, the term "substantially free" in the claims is a relative term, which renders the claim indefinite. The term "substantially" is not defined by the claim, the

specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

As to claim 22, the recitation of the *aqueous* lacks antecedent basis in the claims.

Claim Rejections - 35 USC 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

Claim 25 is rejected under 35 U.S.C. 102(e) as being anticipated by Davis et al. US 4,863,731, 1989.

The claims are drawn to a preparation for the prevention and treatment of coccidiosis comprising: a pharmaceutically acceptable carrier, diluent, or excipient; live sporulated oocysts of at least one species of coccidial protozoa; and an amino acid; wherein the sporulated oocysts are sanitized.

Davis et al teach a composition comprising water (a pharmaceutically acceptable carrier or diluent) and 1,000 to 1,000,000 viable sporulated oocysts of at least one species of coccidian (e.g. *Eimeria* to which poultry are susceptible (column 2 lines 63-68 to column 3 lines 1-15) and one edible thickening agent in an amount to promote

suspension of said oocysts and an amino acid (column 10 claims 1 and 2). Davis et al teach that said oocysts used in said composition were collected from bird droppings and were cleaned by removing undesirable matter via treatment steps involving centrifugation and sedimentation of said oocysts to remove said undesirable matter, thus said oocysts are sanitized (see attached definition of sanitize and column 7 lines 26-48).

Claim 25 is rejected under 35 U.S.C. 102(e) as being anticipated by Williams et al. US 6,146,838, Nov. 14, 2000 filed March 18. 1997.

The claims are drawn to a preparation for the prevention and treatment of coccidiosis comprising: a pharmaceutically acceptable carrier, diluent, or excipient; live sporulated oocysts of at least one species of coccidial protozoa; and an amino acid; wherein the sporulated oocysts are sanitized.

Williams et al teach a composition comprising bleach treated (sanitized, see attached definition of sanitize and column 7 lines 26-48) *Cryptosporidium parvum* oocysts and phosphate buffered saline and the amino acid – cysteine (column 2 lines 29-35).

Claim Rejections - 35 USC 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 2, 3 in-part, 4, 5, 6 in-part, 7 in-part, 11-13, 16-19, 21, 26 and 27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bhogal et al US 4,808,404 1989 in view of Smith et al. Parasitology 1998 vol. 117: S113-S141.

The claims are drawn to a composition comprising viable sporulated oocysts of at least one species of protozoa known to cause coccidiosis, a pharmaceutically acceptable carrier, diluent, or excipient, and at least one surfactant capable of preventing or reducing the aggregation of sporulated oocysts, wherein the composition is sterile wherein said protozoa are of the genus *Eimeria*, wherein said protozoa are selected from the group consisting of *Eimeria acervulina, Eimeria maxima, Eimeria mitis, Eimeria tenella, Eimeria necatrix, Eimeria brunetti, Eimeria praecox*, and wherein said protozoa comprise a plurality of species of protozoa, wherein said plurality of species comprise *Eimeria acervulina, Eimeria maxima, and Eimeria tenella*, wherein said surfactant is selected from the group consisting of non-ionic surfactants, wherein said surfactant is a non-ionic surfactant selected from the group consisting of Tween 20, Tween 80, 16, wherein said composition is substantially free of bacterial contamination, wherein said bacterial contamination is removed by tangential flow filtration, wherein bacterial contaminants have been removed from said composition at one or more step(s) of production, wherein said contaminants are removed by tangential flow filtration 21, wherein the diluent comprises water. And preparation for the prevention

and treatment of coccidiosis comprising: a pharmaceutically acceptable carrier, diluent, or excipient; live sporulated oocysts of at least one species of coccidial protozoa; and a surfactant; wherein the sporulated oocysts are sanitized, wherein the surfactant is selected from the group consisting of ionic detergents and non-ionic detergents.

Bhogal et al teach a composition comprising viable sporulated oocysts of *Eimeria* known to cause coccidiosis and sterile phosphate buffered saline wherein the oocysts have been treated with CHLOROX (column 7 paragraph 5.2.2 especially line 50-51). CHLOROX contains sodium hypochlorite 5.25% see the instantly filed specification p. 68 first sentence of paragraph 194). The instantly filed specification on p.41 paragraph 110 teach that sodium hypochlorite may be used as a sterilization agent at a concentration from about 1%-10% to sterilize the oocysts. Hence, said composition of Bhogal et al contains sodium hypochlorite, which falls within the 1%-10% range, that is required for sterility as stated in the specification. Therefore, the composition of Bhogal et al is also sterile.

Bhogal et al teach that in preparation of the sporulated oocysts composition (which is used to obtain sporozoites), a selection of sporozoites of common species of coccidian should be included in a single formulation when broad host immunity is required. This suggests that the sporulated oocysts preparation can contain a plurality of *Eimeria* species (column 7 lines 4-21) wherein said plurality of species comprises

Eimeria acervulina, Eimeria maxima and Eimeria tenella. Bhogal et al teach that said sterile composition of sporulated oocysts is stored in buffer at 4oC. It is obvious that said composition at a point is exposed to air and eventually stored in a container and that such a container will contain a cap or stopper. Said oocysts are previously treated with bleach CHOLOROX, therefore said composition is substantially free of bacterial contamination. As to claims, 17-19, the claims are product by process claims. Claims 17-19 recite process limitations such as " wherein said bacterial contamination is removed by tangential flow filtration" or " wherein bacterial contaminants have been removed from said composition at one or more step (s) of production" "[E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." In re Thorpe, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985). See MPEP chapter 2113, Product-by-Process claims. Thus, claims 17-19 are drawn to the composition and not to the processes recited in said claims. The sterile phosphate buffered saline in which said sporulated oocysts are stored comprises water.

Bhogal et al does not teach a surfactant in said composition capable of preventing or reducing the aggregation of sporulated oocysts.

Smith et al teach the use of detergent such as Tween™ 20, Tween™ 80, Hyamine™ to discourage parasite ova from clumping and encouraging the detachment of said parasites from sample surfaces and other particulates.

It would have been prima facie obvious to one of skill in the art at the time the invention was made to include a surfactant in the composition of Bhogal et al as taught by Smith et al. The motivation to do so is provided by Smith who teach that detergents such as Tween™ 20, Tween™ 80, Hyamine™ is beneficial in discouraging parasite ova from clumping and encourages the detachment of said parasites from sample surfaces and other particulates.

Claims 1, 2, 3 in-part, 4, 5, 6 in-part, 7 in-part, 11-15. 16-19, 21, 26 and 27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Evans et al WO 96/40233, 1996 in view of Smith et al. Parasitology 1998 vol. 117: S113-S141.

The claims are drawn to a composition comprising viable sporulated oocysts of at least one species of protozoa known to cause coccidiosis, a pharmaceutically acceptable carrier, diluent, or excipient, and at least one surfactant capable of preventing or reducing the aggregation of sporulated oocysts, wherein the composition

is sterile wherein said protozoa are of the genus Eimeria, wherein said protozoa are selected from the group consisting of *Eimeria acervulina, Eimeria maxima, Eimeria mitis, Eimeria tenella, Eimeria necatrix, Eimeria brunetti, Eimeria praecox*, and wherein said protozoa comprise a plurality of species of protozoa, wherein said plurality of species comprise *Eimeria acervulina, Eimeria maxima, and Eimeria tenella*, wherein said surfactant is selected from the group consisting of non-ionic surfactants, wherein said surfactant is a non-ionic surfactant selected from the group consisting of Tween 20, , wherein said aggregation is at an interface, wherein said interface is selected from the group consisting of a composition-air interface, a composition-container interface, or any combination thereof, wherein said aggregation is on a container cap or stopper, wherein said composition comprises one or more dosage unit, wherein each dosage unit comprises not more than about 10times the minimum immunizing dose of said oocysts. Wherein said composition is substantially free of bacterial contamination, wherein said bacterial contamination is removed by tangential flow filtration, wherein bacterial contaminants have been removed from said composition at one or more step(s) of production, wherein said contaminants are removed by tangential flow filtration 21, wherein the diluent comprises water and a preparation for the prevention and treatment of coccidiosis comprising: a pharmaceutically acceptable carrier, diluent, or excipient; live sporulated oocysts of at least one species of coccidial protozoa; and a

surfactant; wherein the sporulated oocysts are sanitized, wherein the surfactant is selected from the group consisting of ionic detergents and non-ionic detergents.

Evans et al teach a composition comprising viable sporulated oocysts of two or more *Eimeria* species (e.g. *tenella, acervulina, maxima*) known to cause coccidiosis, phosphate buffered saline wherein the oocysts have been treated with 50% sodium hypochlorite (p.6 lines 16-19), hence, said composition is sterile (p.3 line 15, p. 4 line 9-19, p. 6 line16-19, p. 6 line 31-33, p.7 line 3-8, p. 8 claim 8). The instant specification on p.41 paragraph 110 teach that sodium hypochlorite may be used at a concentration from about 1%-10% to sterile the oocysts. Evans teaches 50% sodium hypochlorite; therefore Evans concentration of sodium hypochlorite surpasses the instant range 1%-10%. Thus, both the instant composition and the composition of Evans are sterile whether 1-10% or 50% sodium hypochlorite is used.

Evans et al teach that said composition of sporulated oocysts is used as a vaccine and injected into eggs. Evans et al also teach the preparation of said composition of sporulated oocysts and that it is stored under refrigeration until needed (p.6 lines 1-10) It is obvious that said composition at a point is exposed to air and eventually stored in a container (e.g. for the purposes of refrigeration) and that such a container will contain a cap or stopper. Evans et al teach said composition having a dose of sporulated oocyst ranging from 10^2 to 10^8 oocysts per dose. Said oocysts are

previously treated with bleach therefore said composition is substantially free of bacterial contamination. As to claims, 17-19, the claims are product by process claims. Claims 17-19 recite process limitations such as " wherein said bacterial contamination is removed by tangential flow filtration" or " wherein bacterial contaminants have been removed from said composition at one or more step (s) of production" "[E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." In re Thorpe, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985). See MPEP chapter 2113, Product-by-Process claims. Thus, claims 17-19 are drawn to the composition and not to the processes recited in said claims. The sterile phosphate buffered saline in which said sporulated oocysts are stored comprises water. Evans et al teach that said composition of sporulated oocysts is used as a vaccine against coccidiosis caused by Eimeria species.

Evans et al does not teach a surfactant in said composition capable of preventing or reducing the aggregation of sporulated oocysts.

Smith et al teach the use of detergent such as Tween™ 20, Tween™ 80, Hyamine™ to discourage parasite ova from clumping and encouraging the detachment of said parasites from sample surfaces and other particulates.

It would have been prima facie obvious to one of skill in the art at the time the invention was made to include a surfactant in the composition of Evans et al as taught by Smith et al. The motivation to do so is provided by Smith who teach that detergents such as Tween™ 20, Tween™ 80, Hyamine™ is beneficial in discouraging parasite ova from clumping and encourages the detachment of said parasites from sample surfaces and other particulates.

Claims 1, 2, 3 in-part, 4, 5, 6 in-part, 7 in-part, 11-15 16-19, 21-24, 26 and 27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Evans et al WO 96/40233, 1996 and Smith et al. Parasitology 1998 vol. 117 :S113-S141 further in view of Dibner et al US 6,344,340, 2002 (provisional application filed March 1, 1999) and Clark et al. PNAS vol. 93, p. 6825-6829, 1996.

The claims are drawn to a composition comprising viable sporulated oocysts of at least one species of protozoa known to cause coccidiosis, a pharmaceutically acceptable carrier, diluent, or excipient, and at least one surfactant capable of

preventing or reducing the aggregation of sporulated oocysts, wherein the composition is sterile wherein said protozoa are of the genus *Eimeria*, wherein said protozoa are selected from the group consisting of *Eimeria acervulina, Eimeria maxima, Eimeria mitis, Eimeria tenella, Eimeria necatrix, Eimeria brunetti, Eimeria praecox*, and wherein said protozoa comprise a plurality of species of protozoa, wherein said plurality of species comprise *Eimeria acervulina, Eimeria maxima, and Eimeria tenella*, wherein said surfactant is selected from the group consisting of non-ionic surfactants, wherein said surfactant is a non-ionic surfactant selected from the group consisting of Tween 20, , wherein said aggregation is at an interface, wherein said interface is selected from the group consisting of a composition-air interface, a composition-container interface, or any combination thereof, wherein said aggregation is on a container cap or stopper, wherein said composition comprises one or more dosage unit, wherein each dosage unit comprises not more than about 10 times the minimum immunizing dose of said oocysts, wherein said composition is substantially free of bacterial contamination, wherein said bacterial contamination is removed by tangential flow filtration, wherein bacterial contaminants have been removed from said composition at one or more step(s) of production, wherein said contaminants are removed by tangential flow filtration 21, wherein the diluent comprises water, wherein the aqueous diluent comprises 0.5.times phosphate buffered saline further comprising gentamicin, wherein

said gentamicin is present in an amount of about 30 microgram/ml and a preparation for the prevention and treatment of coccidiosis comprising: a pharmaceutically acceptable carrier, diluent, or excipient; live sporulated oocysts of at least one species of coccidial protozoa; and a surfactant; wherein the sporulated oocysts are sanitized, wherein the surfactant is selected from the group consisting of ionic detergents and non-ionic detergents.

The combination of Evans et al and Smith et al is set forth supra. Said combination does not teach 0.5X phosphate buffered saline (PBS) and gentamicin in their combined composition.

Dibner et al teach a composition of sporulated oocysts in PBS containing 30 microgram/mL gentamicin or other acceptable disinfectant (column 8 last sentence).

Clark et al teach a composition of protozoan parasites in 0.5X PBS (p. 6826 left column under immunofluoresence microscopy).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to include gentamicin and 0.5x PBS in the composition of Evans and Smith et al as taught by Dibner et al and Clark et al because Dibner et al teach a composition of sporulated oocysts in PBS containing gentamicin wherein gentamicin is used as a disinfectant and Clark et al teach a composition of protozoan parasites in 0.5X PBS and PBS is generally used in the art as a buffer/diluent.

Claims 1, 2, 3 in-part, 4, 5, 6 in-part, 7 in-part, 11-13, 16-19, 21-24, 26 and 27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bhogal et al US 4,808,404 1989 and of Smith et al. Parasitology 1998 vol. 117: S113-S141 further in view of Dibner et al US 6,344,340, 2002 (provisional application filed March 1, 1999) and Clark et al. PNAS vol. 93, p. 6825-6829, 1996.

The claims are drawn to a composition comprising viable sporulated oocysts of at least one species of protozoa known to cause coccidiosis, a pharmaceutically acceptable carrier, diluent, or excipient, and at least one surfactant capable of preventing or reducing the aggregation of sporulated oocysts, wherein the composition is sterile wherein said protozoa are of the genus *Eimeria*, wherein said protozoa are selected from the group consisting of *Eimeria acervulina, Eimeria maxima, Eimeria mitis, Eimeria tenella, Eimeria necatrix, Eimeria brunetti, Eimeria praecox*, and wherein said protozoa comprise a plurality of species of protozoa, wherein said plurality of species comprise *Eimeria acervulina, Eimeria maxima, and Eimeria tenella*, wherein said surfactant is selected from the group consisting of non-ionic surfactants, wherein said surfactant is a non-ionic surfactant selected from the group consisting of Tween 20, , wherein said aggregation is at an interface, wherein said interface is selected from the group consisting of a composition-air interface, a composition-container interface, or any combination thereof, wherein said aggregation is on a container cap or stopper,

wherein said composition comprises one or more dosage unit, wherein each dosage unit comprises not more than about 10 times the minimum immunizing dose of said oocysts, wherein said composition is substantially free of bacterial contamination, wherein said bacterial contamination is removed by tangential flow filtration, wherein bacterial contaminants have been removed from said composition at one or more step(s) of production, wherein said contaminants are removed by tangential flow filtration 21, wherein the diluent comprises water, wherein the aqueous diluent comprises 0.5.times. phosphate buffered saline further comprising gentamicin, wherein said gentamicin is present in an amount of about 30 microgram/ml and a preparation for the prevention and treatment of coccidiosis comprising: a pharmaceutically acceptable carrier, diluent, or excipient; live sporulated oocysts of at least one species of coccidial protozoa; and a surfactant; wherein the sporulated oocysts are sanitized, wherein the surfactant is selected from the group consisting of ionic detergents and non-ionic detergents.

The combination of Bhogal et al and Smith et al is set forth supra. Said combination does not teach 0.5X phosphate buffered saline (PBS) and gentamicin in their combined composition.

Dibner et al teach a composition of sporulated oocysts in PBS containing 30 microgram/mL gentamicin or other acceptable disinfectant (column 8 last sentence).

Clark et al teach a composition of protozoan parasites in 0.5X PBS (p. 6826 left column under immunofluoresence microscopy).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to include gentamicin in the composition of Bhogal and Smith et al as taught by Dibner et al and Clark et al because Dibner et al teach a composition of sporulated oocysts in PBS containing gentamicin wherein gentamicin is used as a disinfectant and Clark et al teach a composition of protozoan parasites in 0.5X PBS and PBS is generally used in the art as a buffer/diluent.

Claims 1, 2, 3 in-part, 4, 5, 6 in-part, 7 in-part, 8-10,11-13, 16-19, 21, 26 and 27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bhogal et al US 4,808,404 1989 and Smith et al. Parasitology 1998 vol. 117 :S113-S141 further in view of Jensen et al US 2004/0248793, Dec. 2004 – provisional application dated Jun. 30, 2003.

The claims are set forth supra. The combination of Bhogal et al and Smith et al (set forth supra) does not teach surfactant concentrations of from about 0.05 mg/ml to about 10 mg/ml or 0.05 mg/ml to 2.0 mg/ml or 0.1 mg/ml to 2mg/ml.

Jensen et al teach surfactant used for stabilizing a pharmaceutical composition wherein said surfactants are added in the amount form 0.005 to 5mg/mL or 0.01 to 3 mg/mL (p. 10 paragraph 128). Jensen et al further teach that surfactants include those agents, which protect against aggregation (p. 7 paragraph 86).

It would have been prima facie obvious to one of skill in the art at the time the invention was made to use the concentration range of surfactants in the composition of Bhogal and Smith et al as taught by Jensen et al. The motivation to do so is provided by Smith et al and Jensen el. Smith et al teach that detergents such as Tween™ 20, Tween™ 80, Hyamine™ is beneficial in discouraging parasite ova from clumping and encourages the detachment of said parasites from sample surfaces and other particulates and by Jensen who teach different concentrations (0.005 to 5mg/mL or 0.01 to 3 mg/mL) of surfactant that can be used to stabilize a composition and thus reduce aggregation.

Claims 1, 2, 3 in-part, 4, 5, 6 in-part, 7 in-part, 8-10,11-15 16-19, 21, 26 and 27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Evans et al WO 96/40233, 1996 and Smith et al. Parasitology 1998 vol. 117 :S113-S141 in view of

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Status of the Claims

Claims 1, 2, 3 in-part, 4, 5, 6 in-part, 7 in-part, 8 - 27 are rejected.

Conclusion

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Oluwatosin Ogunbiyi whose telephone number is 571-272-9939. The examiner can normally be reached on M-F 8:30 am - 5:00 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner' s Supervisory Examiner Jeffery Siew can be reached on 571-272-0787.

The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Oluwatosin Ogunbiyi
Examiner
Art Unit 1645

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PRIMARY EXAMINER